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188

05/03/91

☐ This application has been examined ☒ Responsive to communication filed on 2/11/91 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> _____ |

Part II SUMMARY OF ACTION

1. ☒ Claims 35-41 + 53-62 are pending in the application.

Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 35-41 + 53-62 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).

12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received

☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

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The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 35-39 and 53-59 are rejected under 35 U.S.C. § 102(a) as being anticipated by the MBR product information sheet as set forth in the previous office action of 9/4/90.

Applicants have filed a 37 CFR §1.131 Declaration containing a copy of a description of a Taq polymerase purification protocol and a stabilized enzyme composition supplied to MBR prior to 5/1/87. However, the declaration is defective in being signed by only one co-inventor. One of joint inventors may make the declaration only when the claim rejected is the invention of only this inventor or it is not possible to produce the other joint inventors(MPEP 715.04).

The declaration is further inadequate in that the description relied on as evidence fails to set forth that the nonionic polymeric detergent stabilizes the thermostable nucleic acid polymerase enzyme during storage. In the description of purifying the thermostable polymerase, the diluent and nonionic detergent therein are being used in carrying out a process of purification. The formation of a composition is only incidental to carrying out the process, and the composition is not being prepared with the objective of producing a composition that is stable during storage. While the last page of the description, discloses a 2X storage buffer containing a nonionic detergent as asserted by applicants, there is no recognition in the

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description that the nonionic detergent is functioning to stabilize a thermostable polymerase during storage. The nonionic detergent could have been used for another function such as to prevent aggregation as disclosed by Goff et al (col 20, lines 24-
5 25). Storage stability could have been believed to result from the glycerol, DTT and other components present in the 2X storage buffer. The 2X storage buffer contains components and proportions not required by the present claims and not contained by the MBR storage buffer. For example, the 2X buffer contains
10 NP40 and Tween 20 whereas the MBR buffer contains only Tween 20, and the proportions of all components of the MBR buffer are different from the proportions of the components of the 2X buffer. Thus, the MBR buffer is a species different from the 2X buffer and both are within the scope of the present claims. In
15 chemical cases, where generic claims have been rejected on a reference which discloses a species not antedated by the affidavit or declaration, the rejection is not withdrawn (MPEP 715.03).

Claims 40, 41 and 60-62 are rejected under 35 U.S.C. § 103
20 as being unpatentable over the product information sheet of MBR for reasons set forth in the previous office action.

As noted above, the 37 CFR §1.131 Declaration fails to obviate the MBR reference.

Claims 1, 35-41, 53-59 and 62 are rejected under 35 U.S.C.
25 § 103 as being unpatentable over Kaledin et al (1980) in view of

Goff et al and, if necessary, in further view of Feller et al or Spiegelman for reasons set forth in the previous office action.

Applicant's arguments filed 2/11/91 have been fully considered but they are not deemed to be persuasive.

5 Applicants urge that Kaledin et al believed that any problem of thermostable polymerase stability had been solved since the introduction of gelatin was disclosed to stabilize enzymatic activity, and there is no motivation to change the formulation of the reference to overcome a problem of stability. However, when
10 Goff et al and, if needed, Feller et al or Spiegelman are considered, it would have been apparent that in addition to gelatin a nonionic detergent would have also functioned to stabilize the polymerase. To use an alternative stabilizing agent known for polymerase stabilization would have been a matter
15 of obvious choice depending on individual preference and convenience. Furthermore, to select a preferred stabilizing agent from these known would have required only limited routine experimentation and have been within the skill of the art. In any event, Goff et al disclose(col 20, line 25) that in addition
20 to preventing loss of activity the nonionic detergent prevents aggregation. This would have been an additional result obtained from using a nonionic detergent that would have been a motivation to select the detergent rather than gelatin for stabilizing. Furthermore, the nonionic detergent of Goff et al is present in a
25 buffer used during lysis(col 20, line 21) and other purification

steps, and for storage of the enzyme. This use of the detergent in multiple stages would have been motivation for its use rather than gelatin which is used only in one stage.

Applicants urge that Goff et al recover reverse
5 transcriptase enzyme and does not suggest stability problems associated with thermostable polymerase. However, reverse transcriptase is a DNA polymerase enzyme(Feller et al(col 1, lines 65-68)), and Goff et al clearly disclose using a nonionic detergent to maintain activity. It would have been obvious that
10 the nonionic detergent would have maintained the activity of DNA polymerase in the absence of something to lead one to believe the contrary. There is seen nothing to lead one to believe that a polymerase being thermostable changes its characteristics so as to make unexpected a nonionic detergent functioning to stabilize
15 the enzyme as suggested by Goff et al and, if needed, Feller et al or Spiegelman. Being thermostable merely means that the DNA polymerase is stable at a higher temperature. Such a polymerase would otherwise be expected to have the characteristics and function of other DNA polymerase. It is clearly apparent from
20 Kaledin et al(1980), as well as Kaledin et al(1981), that thermostable DNA polymerase loses activity like other DNA polymerase as disclosed by other references without a stabilizing agent being present. The type of comments set forth above in response to applicants' arguments concerning Goff et al also
25 apply to Feller et al and Spiegelman.

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Claims 60 and 61 are rejected under 35 U.S.C. § 103 as being unpatentable over the references as applied to claims 1, 35-41, 53-59 and 62 above, and further in view of Kaledin et al(1981) or Ruttimann et al(1985) for reasons set forth in the previous office action.

The type of comments set forth above in response to arguments also apply to this rejection.

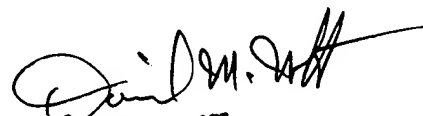
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Examiner Naff at telephone number (703) 308-0520.

David M. Naff
May 1, 1991


DAVID M. NAFF
PRIMARY EXAMINER
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